IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Jong-Soo Woo et al.
Serial No.: 10/534,066
Filed: November 7, 2003
For: MICROEMULSION CONCENTRATE FOR ORAL ADMINISTRATION OF WATER-INSOLUBLE ANTI-COLD DRUG AND METHOD FOR PREPARING SAME

Group Art Unit: 1614
Examiner: ROBERTS, LEZAH

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUPPLEMENTAL DECLARATION UNDER 37 C.F.R. SECTION 1.132

I, Jong-Soo WOO, being a citizen of the Republic of Korea and presently residing at Baekseolmaeul 598-1302, Jeongja-dong, Jangan-gu, Suwon-si, Kyungki-do 440-300, Republic of Korea, do declare:

That I am one of the co-inventors of the invention disclosed in the above-identified application, and hence am fully familiar with the subject matter therein; and

That I have conducted a series of comparative experiments to demonstrate unexpectedly improved properties of the microemulsion concentrates prepared by the method disclosed in the subject application, as follows.

In order to determine the solubilities of the active ingredient (<Test 1>), the emulsion stability of the microemulsion pre-concentrate (<Test 2>) and the dissolution rate of the active ingredient (<Test 3>), the inventive microemulsion pre-concentrate of Example 1 (Ibuprofen 200mg/capsule) was examined together with four comparative microemulsion pre-concentrates (ⓐ, ⓑ, ⓒ and ⓓ, respectively) prepared by simultaneously dissolving the same components of Example 1 in ethanol (500mg/capsule), while changing that the amount of Ibuprofen from 200(ⓐ) to 150(ⓑ), 100(ⓒ) and 50(ⓓ)mg/capsule. Specifically, in case of Example 1 of the present invention, ibuprofen was uniformly dissolved in ethanol, and then polyoxyethylene-40-hydrogenated castor oil, Fluronic® L-44NF, Tween® 20 and propyleneglycol monocaprylate were added to the ibuprofen solution in order and dissolved; and in case of comparative experiments, polyoxyethylene-40-hydrogenated castor oil, Fluronic® L-44NF, Tween® 20, propyleneglycol monocaprylate and ibuprofen were added to ethanol in order, and all of them were dissolved.

<Test 1> : Solubility of the active ingredient

The precipitation of the crystalline residues of the active ingredients (Ibuprofen) of the microemulsion pre-concentrates (Example 1, ⓐ, ⓑ, ⓒ and ⓓ) were observed with naked eyes, the observed results being as follows:

	Example 1	ⓐ	ⓑ	ⓒ	ⓓ
crystalline residue	-	+++	++	+	-

(no precipitation: -, small precipitation: +, middle precipitation: ++, large precipitation: +++)

<Test 2> : Emulsion stability test (Precipitation formation test)

In order to examine whether the microemulsion pre-concentrates (Example 1, ⓐ, ⓑ, ⓒ and ⓓ) form precipitates upon contact with an aqueous solution, tests were performed using distilled water, artificial gastric juice and artificial intestinal juice, respectively, with the same method as that disclosed in Test Example 3 of the specification as originally filed. Prior to this test, three comparative microemulsion pre-concentrates, ⓐ, ⓑ and ⓒ, were each passed through a 0.45μm Millex filter to remove crystalline residues contained therein. The observed results are as follows:

	Example 1	ⓐ	ⓑ	ⓒ	ⓓ
Distilled water	-	++	++	+	-
Artificial gastric juice	-	++	++	+	+
Artificial intestinal juice	-	++	++	+	-

(no precipitation: -, small precipitation: +, middle precipitation: ++, large precipitation: +++)

<Test 3> : Dissolution test

The dissolution tests of the microemulsion pre-concentrates (Example 1, ⓐ, ⓑ, ⓒ and ⓓ: 200mg as Ibuprofen) were performed using 900ml of artificial gastric juice (pH 1.2) by the same method as disclosed in Test Example 1 of the specification as originally filed. The amounts of Ibuprofen dissolution measured after 60 min were to the extents of 96%, 12%, 22%, 27% and 29% for Example 1, ⓐ, ⓑ, ⓒ and ⓓ, respectively.

As can be seen from the above results, it can be concluded that the inventive

microemulsion pre-concentrates exhibit higher performance characteristics in terms of active ingredient solubility, emulsion stability and dissolution rate than the comparative microemulsion pre-concentrates. Therefore, the inventive microemulsion concentrate can form stable emulsified drug microparticles upon contact with a body fluid, thereby providing constant bioavailability without any change of the emulsified state by pH variation.

The undersigned declarant further declares that all statement made therein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Dated: June 25, 2007

By: Jong Soo Woo

Jong-Soo WOO